2.0 DESCRIPTION OF PROPOSED RESEARCH IN NON-TECHNICAL LANGUAGE

Cystic fibrosis (CF), the most common inherited disease in North America, is caused by problems in a gene known as "CFTR". Normal functioning of this gene is required for the movement of water and salt across airway cells. Persons with this disease have abnormal mucous in their lungs and sinuses which builds up over time and leads gradually, over many years, to serious lung disease and chronic sinusitis, respectively. Attempts are being made to replace the missing gene function using special gene carriers, or vectors, which carry corrected genes into cells. The types of vectors tested in patients so far have a temporary effect and therefore may not be ideal for treating CF lung disease. Targeted Genetics Corporation has developed a different type of vector, called tgAAVCF, which is based on a virus, AAV, that is able to maintain its DNA for long periods of time in the cells that it enters. This vector may provide long term correction of the biological defect seen in cystic fibrosis patients. Our tests of AAV vectors carrying the CFTR gene have shown it to be biologically active in cells in the test tube and in animals, and safe in animals.

One of the many complications of CF is chronic sinusitis. The study described herein proposes to administer tgAAVCF to the maxillary sinuses of patients with CF. Following the determination of an appropriate dose of tgAAVCF, patients currently undergoing monthly antibiotic instillation into their sinuses, will in lieu of their current therapy have tgAAVCF placed in one maxillary sinus and placebo (salt water) in their other sinus through a small plastic tube. This clinical trial will be performed in adult men and women with CF, in order to determine whether a functioning CFTR gene can decrease the likelihood of patients developing symptoms of sinusitis in the sinus treated with tgAAVCF when compared to the sinus receiving placebo. We hope to use these results in order to design future studies which will attempt to actually treat or prevent disease in people with CF.